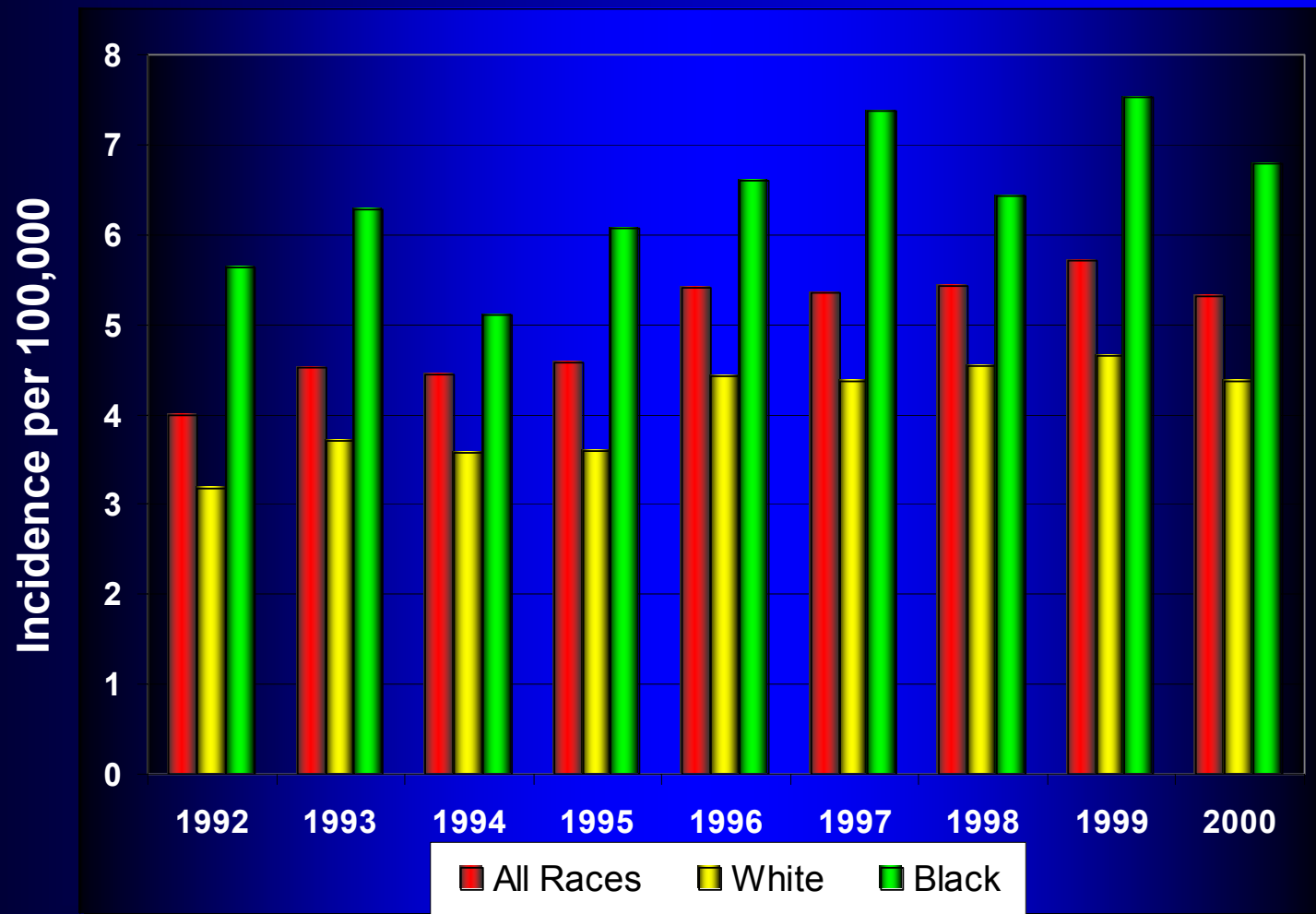


NCI Initiatives in Liver Cancer Research

**Liver Disease Subcommittee Meeting
Digestive Diseases Interagency Coordinating Committee (DDICC)
November 25, 2003**

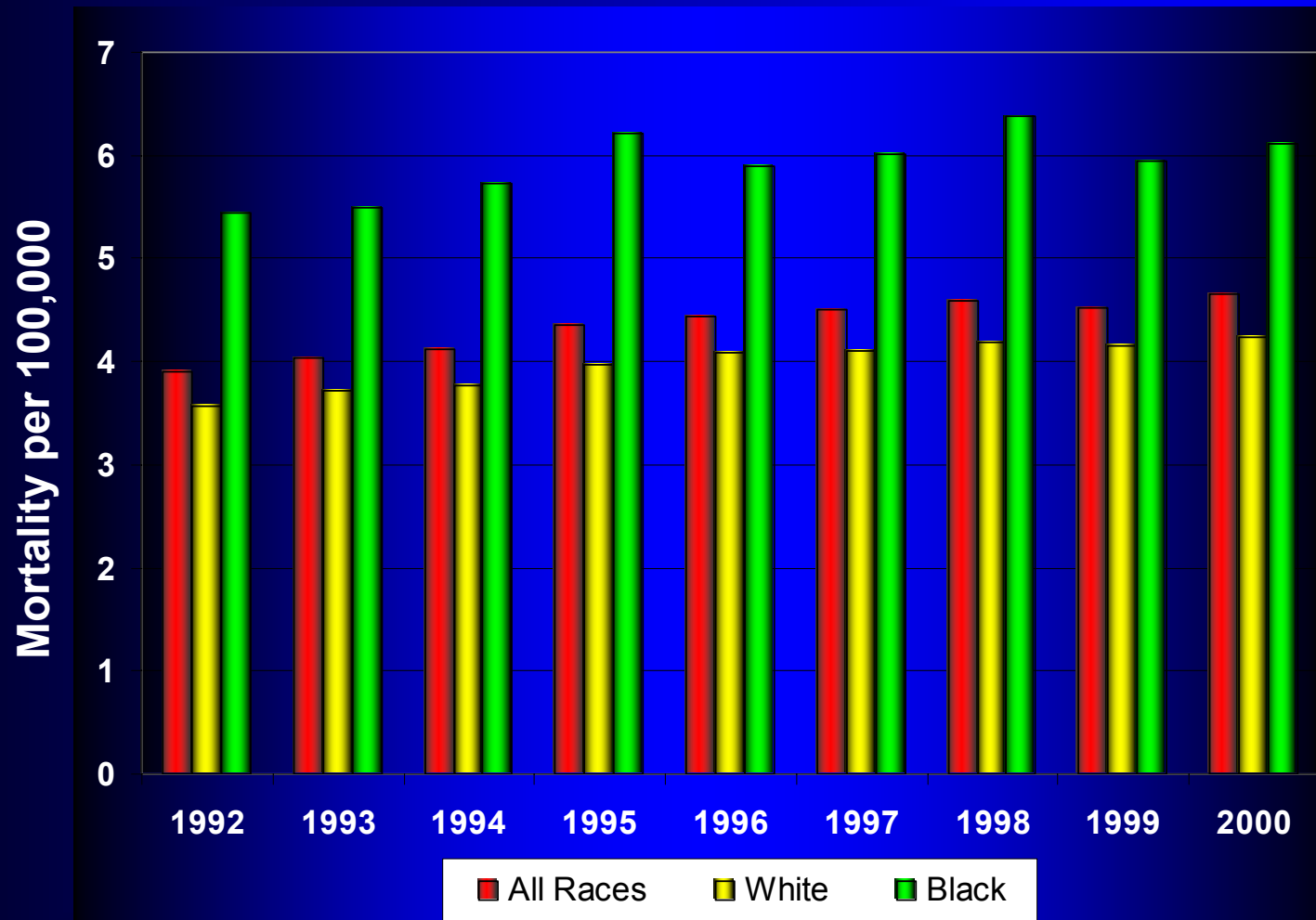
**Jaye L. Viner, MD, MPH
Division of Cancer Prevention
National Cancer Institute, NIH, DHHS**

U.S. Liver & Intrahepatic Bile Duct Cancer Incidence 1992 - 2000



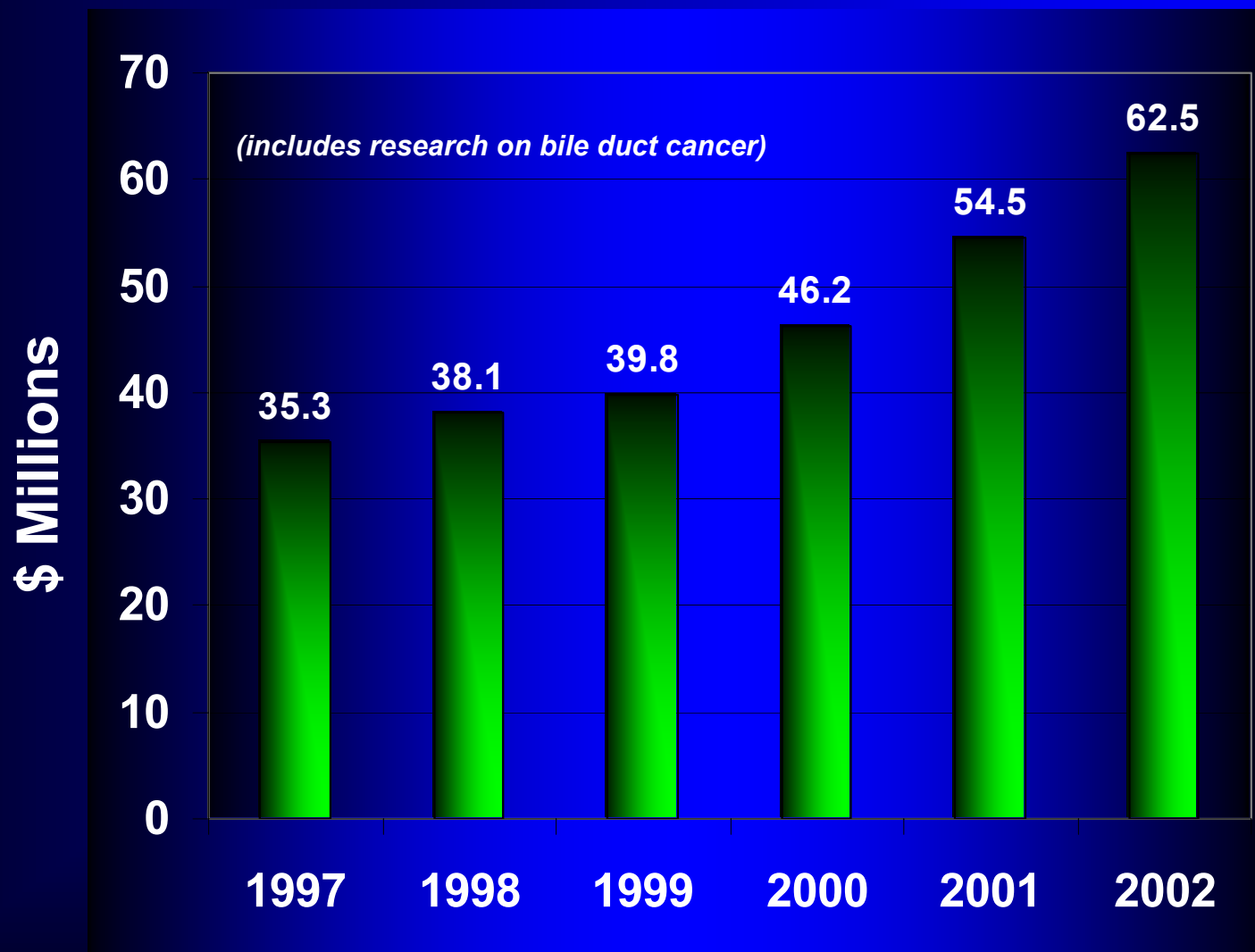
Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov)

U.S. Liver & Intrahepatic Bile Duct Cancer Mortality 1992 - 2000

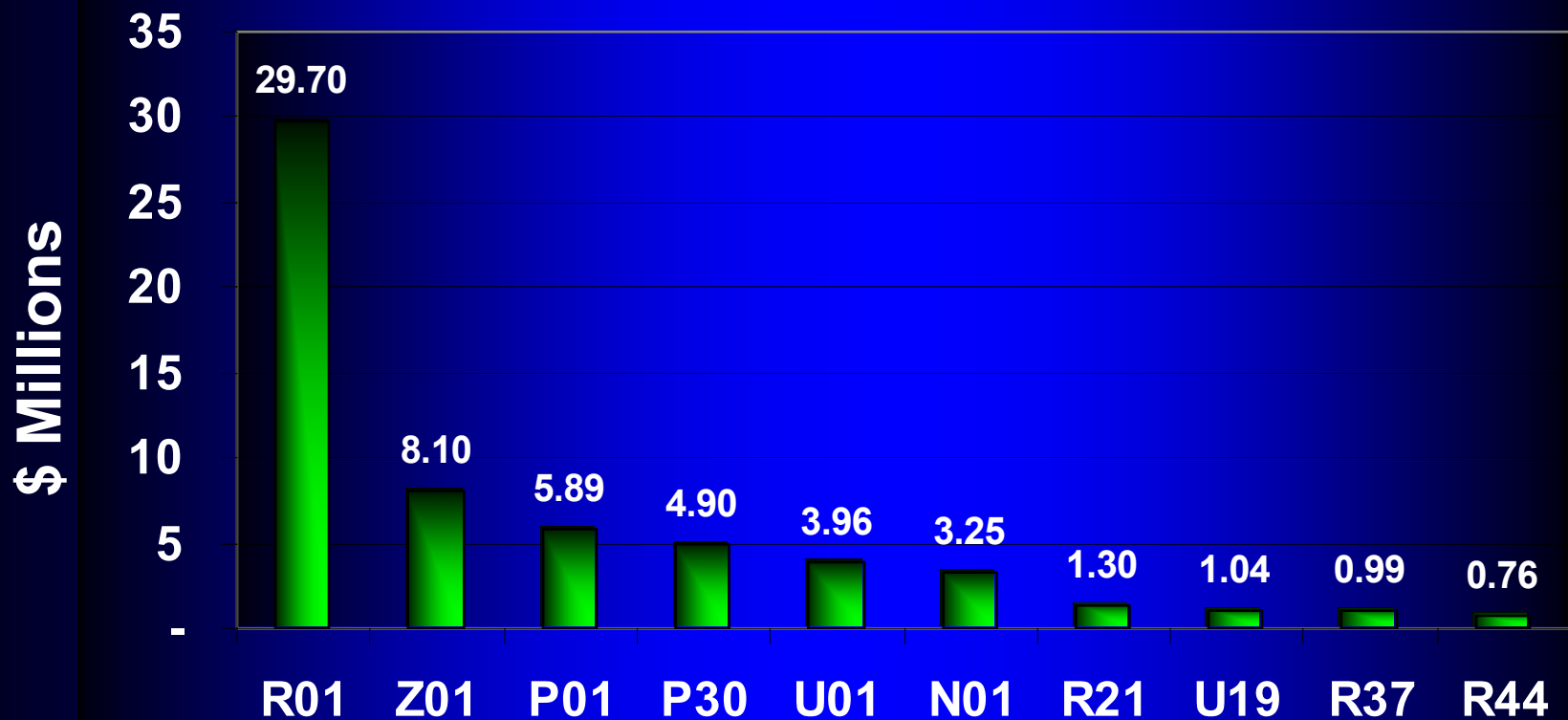


Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov)

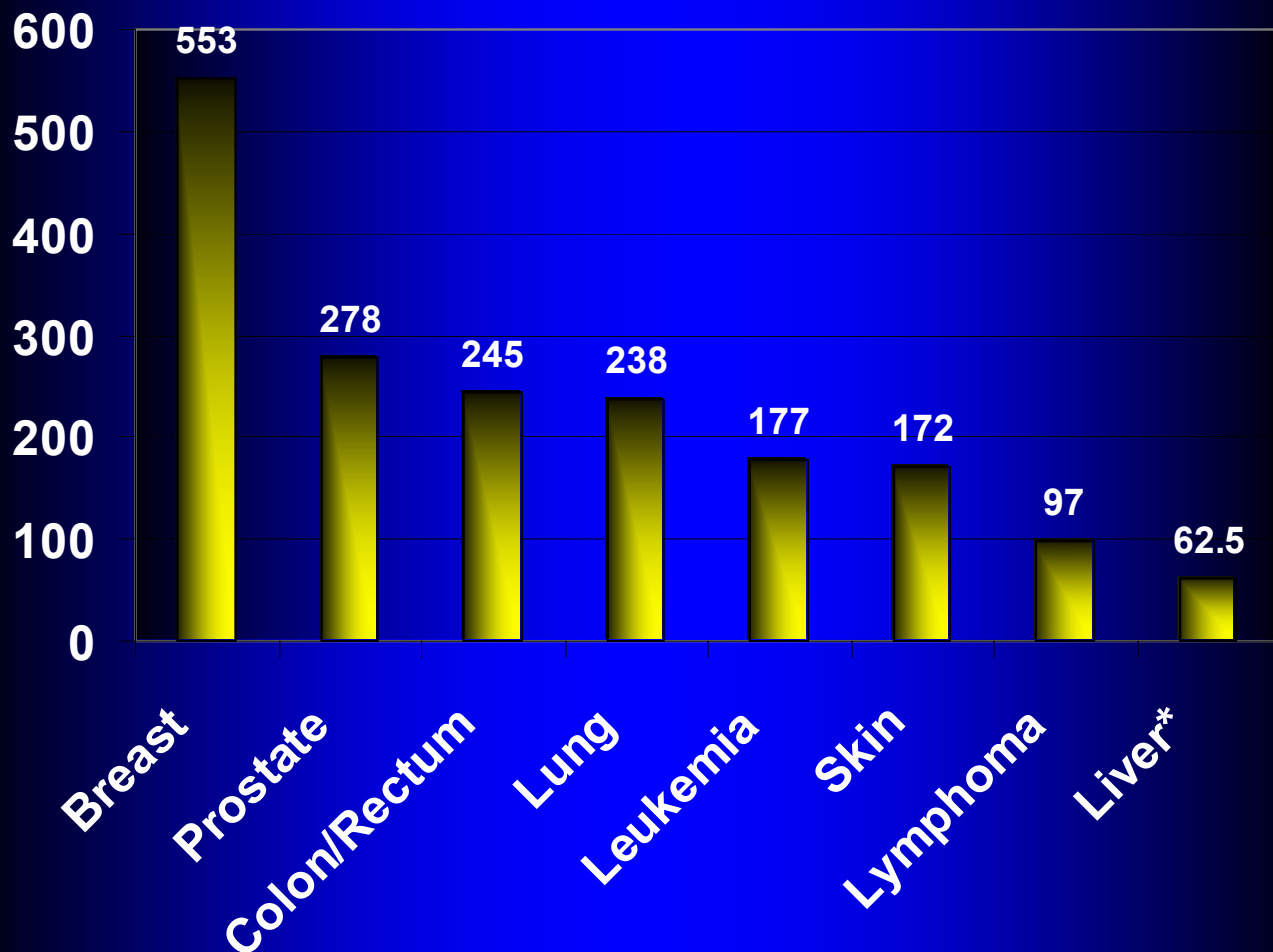
NCI Liver Cancer Research Investment 1997 - 2002



NCI Liver Cancer Research Portfolio FY2002 by Funding Mechanism



NCI FY 2002 Funding (\$ millions)



**Includes bile duct cancer*

Primary Hepatocellular Carcinoma (HCC)

- **500,000 deaths annually worldwide¹**
 - 80% in developing countries (SE Asia, sub-Saharan Africa)
- **Risk factors**
 - Chronic infections (HBV, HCV)
 - Alcohol
 - Dietary contaminants (e.g., aflatoxin)
- **Geographic variation**
 - Immigration from high prevalence regions
- **Rapidly increasing rates in the U.S.**
 - HCV epidemic peak ~1980s²
 - High rates of malignant transformation
- **Long latency between exposure & the development of invasive disease**
 - Opportunities for risk stratification
 - Application of prophylactic & therapeutic interventions

¹McGlynn KA et al; *Int J Cancer* 2001

²Armstrong GL et al; *Hepatology* 2000; El-Serag HB, et al: *Ann Intern Med*, 2003

NCI Liver Disease Research

- **Initiatives**

- **Cancer Cooperative Groups**
- **Children's Oncology Group**
- **Early Phase Trials Consortium**
- **Early Detection Research Network (EDRN)**
- **HALT-C Trial (NIDDK, NCI)**
- **Multi-Institute RFA, PA**
 - **Hepatitis C: Natural History, Pathogenesis, Therapy and Prevention**
 - **Hepatitis C Working Group**

Current NCI-Sponsored Phase I & I/II Trials

Trial	Participants
Arsenic Trioxide in Patients with Hepatocellular Carcinoma (HCC)	≥12*
Erlotinib in Patients with Unresectable HCC and Moderate Hepatic Dysfunction	12-24
Hepatic Arterial Infusion with Melphelan in Patients with Unresectable Cancer of the Liver	≤36
Alpha-Fetoprotein Peptide-Pulsed Autologous Dendritic Cells in HLA-A*0201-Positive Patients With HCC	12-18 [#]
Epirubicin and Celecoxib in Patients with HCC	3-52 [#]
Gemcitabine and Pemetrexed Disodium in Patients with Unresectable or Metastatic Biliary Tract or Gallbladder Cancer	86 [#]
Oblimersen and Doxorubicin in Patients with Advanced HCC or Other Incurable Solid Tumor	12-18; 15-30 [#]

Source: <http://www.cancer.gov>

*NCI + pharmaceutical sponsor
#Phase I/II trial

Current NCI-Sponsored Phase II Trials

Trial	Participants
Bevacizumab in Patients with Unresectable Nonmetastatic HCC without Main Portal Vein Invasion	18-46
Bevacizumab in Patients with Unresectable HCC Receiving Chemoembolization	30
BAY 43-9006 in Patients with Advanced Inoperable HCC	26-135*
BMS-247550 in Patients with Hepatobiliary Cancer	21-50
Chemoembolization in Patients with Unresectable HCC or Neuroendocrine Hepatic Metastases	19-42
Cisplatin, Doxorubicin, and Tamoxifen (CAT) in Patients with Incurable Soft Tissue Sarcoma, Glioma, Mesothelioma, Hepatoma, Thyroid Cancer, or Adrenal Cancer	14-30**

Source: <http://www.cancer.gov>

*NCI + pharmaceutical sponsor
#Phase I/II trial

Current NCI-Sponsored Phase II Trials

Trial	Participants
Epirubicin and Thalidomide in Patients with Locally Unresectable or Metastatic HCC	12/yr*
Erlotinib in Patients with Unresectable HCC	≤100
Gefitinib in Patients with Advanced Unresectable HCC	23-59
Gemcitabine and Docetaxel in Patients with Unresectable or Metastatic HCC	22-40
Hepatic Arterial Infusion of Yttrium Y 90 Glass Microspheres (TheraSphere) in Patients with Unresectable HCC	≤15
Isolated Hepatic Perfusion with Melphalan in Patients with Primary Unresectable Liver Cancer or Metastases to the Liver	≤ 67
Oxaliplatin in Patients with HCC	18-32

Source: <http://www.cancer.gov>

*NCI + pharmaceutical sponsor
#Phase I/II trial

Current NCI-Sponsored Phase II, II/III & III Trials

Trial	Participants
Radiofrequency Interstitial Ablation in Patients With Primary or Metastatic Liver Cancer Who Are Not Candidates for Surgical Resection	32
Rebeccamycin Analogue in Patients With Advanced Hepatobiliary Carcinoma	12-37
T900607 in Patients With Chemotherapy-Naïve Unresectable HCC	20-35*
Thalidomide in Patients With Unresectable HCC Who Are Undergoing Chemoembolization With Doxorubicin	75
Randomized Study of Intrahepatic Doxorubicin-Magnetic Targeted Carrier Complex Versus IV Doxorubicin in Patients With Unresectable HCC	240**
Randomized Study of T138067 Sodium Versus Doxorubicin in Patients With Chemotherapy-Naïve, Unresectable HCC	750**
Nolatrexed Dihydrochloride Versus Doxorubicin in Patients with Unresectable or Recurrent HCC	446*

Source: <http://www.cancer.gov>

*NCI + pharmaceutical sponsor

#Phase II/III trial

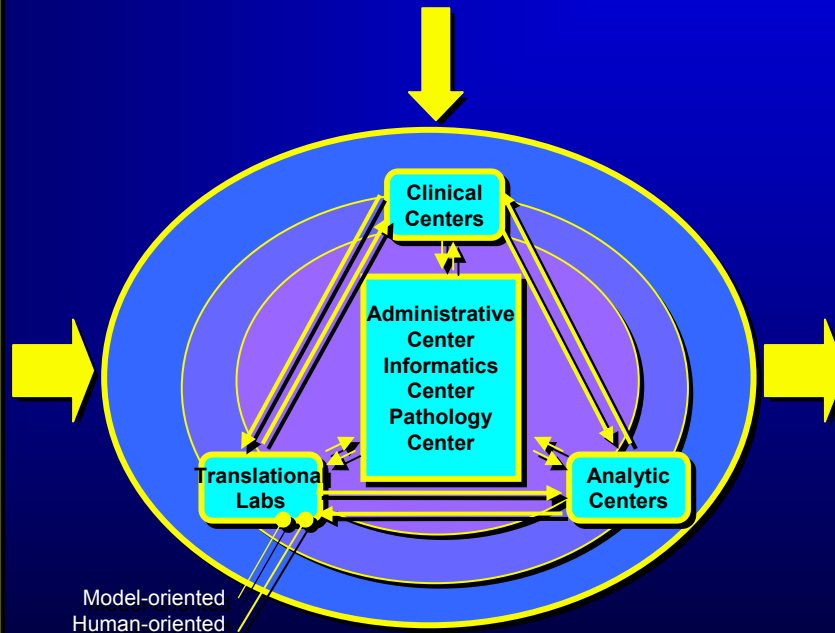
Partnerships for GI Research: Gastrointestinal Translational Research Network (GITRNet)

Foundational Principles

- Translationally-focused
- Product-oriented (business model)
- Mutual interdependence
- Linked informatics
- Synergistic with existing institutions

Research Priorities

- Population studies
- Prevention
- Patient/provider education
- Therapy
- Therapeutic targets
- Markers & molecular profiling
- Outcomes
- Host/environment interactions
- Technologies for screening/surveillance
- Preclinical models



Research Products to Improve Patient Care & Public Health

- Mechanistic insights
- Molecular targets
- Risk measures
- New devices
- New interventions
- New outcome measures
- Patient & provider education